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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/287,500	04/07/1999	JOHN C. LEE	STK-1-DIV-3	6377

7590

03/24/2005

JAMES F HALEY
FISH & NEAVE
1251 AVENUE OF THE AMERICAS
NEW YORK, NY 10020

EXAMINER

ROMEO, DAVID S

ART UNIT

PAPER NUMBER

1647

DATE MAILED: 03/24/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/287,500

Applicant(s)

LEE ET AL.

Examiner

David S. Romeo

Art Unit

1647

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 12 January 2005.
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 69-73, 102, 108-110 and 115-122 is/are pending in the application.
- 4a) Of the above claim(s) 70, 72, 73 and 118-122 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 69, 71, 102, 108-110 and 115-117 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☒ Claim(s) 69-73, 102, 108-110 and 115-122 are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- ☒ Notice of References Cited (PTO-892)
- ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____
- ☒ Interview Summary (PTO-413)
Paper No(s)/Mail Date. 200503.
- ☐ Notice of Informal Patent Application (PTO-152)
- ☐ Other: _____

HL

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is
5 eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 01/12/2005 has been entered.

Election/Restrictions

10 Claims 69, 70, 71, 72, 73, 102, 108, 109, 110, 115, 116, 117, 118, 119, 120, 121, 122 are pending. Applicant's election with traverse of group I, claims 69-73 and 102 to the extent that they are drawn to a method of inducing local tissue formation comprising implanting a morphogenic protein and IGF-I, in Paper No. 21 is acknowledged. Claims 118-122 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a
15 nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 21. Applicant's election of the species bone defect locus, the species fracture, and the species BMP-7 in Paper No. 21 is acknowledged. Claims 70, 72, 73 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected species, there being no allowable generic or linking
20 claim. Claims 69, 71, 102, 106, 108, 115-117 are being examined to the extent that they read upon a method of inducing local tissue formation comprising implanting a morphogenic protein and IGF-I, and the species bone defect locus, the species fracture, and the species BMP-7.

Proposed Examiner's Amendment

The examiner discussed a proposed examiner's amendment with Applicants' representative Connie Wong. See the attached interview summary. Applicants agreed to the examiner's amendment if it would put the case in condition for allowance. However, the
5 examiner was unaware of double patenting issues that remain unresolved in the present application. These issues must be resolved before the case can be allowed.

Maintained Formal Matters, Objections, and/or Rejections:

Double Patenting

10 Claims 69, 71, 102, 108-110, 115-117 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-15 of U.S. Patent No. 6,048,964. It is acknowledged that Applicants are ready to submit a terminal disclaimer when the present claims are found allowable.

15 Claims 69, 71, 102, 108-110, 115-117 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 30 of U.S. Patent No. 5948428. It is acknowledged that Applicants are ready to submit a terminal disclaimer when the present claims are found allowable.

Claim Rejections - 35 USC § 112

Claims 69, 71, 102, 108-110, 115-117 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of synergistically enhancing the ability of OP-1 to induce bone tissue, does not reasonably provide enablement for a method of synergistically enhancing the ability of OP-1 to induce cartilage, tendon/ligament, and neural tissue. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Applicants argue that they have clearly demonstrated that AP activity in vitro correlates with bone induction in vivo. Applicant's arguments have been fully considered but they are not persuasive. While the examiner does not agree that AP activity accurately predicts in vivo osteogenic potential, the evidence [see Yeh (Endocrinology. 1997 Oct;138(10):4181-90) below] nevertheless indicates that IGF-I synergistically stimulates OP-1's ability to induce bone tissue formation from a progenitor cell. Furthermore, the claims are directed to or encompass the synergistic induction of cartilage, tendon/ligament, and neural tissue. However, there is nothing in the prior art of record or in the present specification that establishes a nexus between the induction of alkaline phosphate activity in FRC cells and the induction of cartilage, tendon/ligament, and neural tissue or the synergistic induction thereof. It is noted that claim 71 only limits the locus and not the tissue synergistically induced. It is further noted that claims 109 and 110 only refer to a property of the OP-1 and do not limit the tissue synergistically induced.

Conclusion

Although Wang (B, Paper No. 7) teaches that it is expected that a BMP-2 may act in concert with or perhaps synergistically with other related proteins and growth factors (column 6, lines 5-57; column 7, lines 7-42), Kuberasampath (E, Paper No. 7) teaches that morphogens may be administered together with other "co-factors" known to have a beneficial effect on bone remodeling, including IGF-I (column 4, lines 58-65) and that OP-1 is a useful morphogen (paragraph bridging columns 4-5), and Reddi (V, Paper No. 24) teaches that the initiation of bone formation by osteogenin or BMPs is promoted by IGF-1 (page 34, column 2), this prior art is only weak evidence that OP-1 acts in concert with IGF-I to synergistically induce bone formation.

Although Wozney (U, Paper No. 24) teaches that the use of in vitro assay systems has proven not to be predictive of bone formation in vivo (paragraph bridging pages 726-727), and Li (U, the paper mailed 12/15/2004) suggests that although previous studies have shown that alkaline phosphatase expression is a consistent in vitro osteogenic response seen in BMP-responsive cells and usually correlates with the ability of the various BMPs to induce bone formation in vivo, it may not accurately predict in vivo osteogenic potential (paragraph bridging pages 1738-1739), Yeh (Endocrinology. 1997 Oct;138(10):4181-90) teaches that exogenous IGF-I synergistically and dose dependently enhanced OP-1 action in stimulating [3H]thymidine incorporation, alkaline phosphatase activity, PTH-dependent cAMP level, and bone nodule formation in primary cultures of fetal rat calvaria (FRC) cells (Abstract). Yeh's results, especially with respect to proliferation, reasonably correlate with IGF-I's synergistic stimulation of OP-1's ability to induce bone tissue formation from a progenitor cell.

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No claims are allowable.

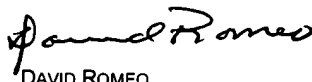
ANY INQUIRY CONCERNING THIS COMMUNICATION OR EARLIER COMMUNICATIONS FROM THE EXAMINER SHOULD BE DIRECTED TO DAVID S. ROMEO WHOSE TELEPHONE NUMBER IS (571) 272-0890. THE EXAMINER CAN NORMALLY BE REACHED ON MONDAY THROUGH FRIDAY FROM 7:30 A.M. TO 4:00 P.M. IF ATTEMPTS TO REACH THE EXAMINER BY TELEPHONE ARE UNSUCCESSFUL, THE EXAMINER'S SUPERVISOR, BRENDA BRUMBACK, CAN BE REACHED ON (571) 272-0961.

IF SUBMITTING OFFICIAL CORRESPONDENCE BY FAX, APPLICANTS ARE ENCOURAGED TO SUBMIT OFFICIAL CORRESPONDENCE TO THE CENTRAL FAX NUMBER FOR OFFICIAL CORRESPONDENCE, WHICH IS (571) 273-8300.

CUSTOMERS ARE ALSO ADVISED TO USE CERTIFICATE OF FACSIMILE PROCEDURES WHEN SUBMITTING A REPLY TO A NON-FINAL OR FINAL OFFICE ACTION BY FACSIMILE (SEE 37 CFR 1.6 AND 1.8).

FAXED DRAFT OR INFORMAL COMMUNICATIONS SHOULD BE DIRECTED TO THE EXAMINER AT (571) 273-0890.

ANY INQUIRY OF A GENERAL NATURE OR RELATING TO THE STATUS OF THIS APPLICATION OR PROCEEDING SHOULD BE DIRECTED TO THE GROUP RECEPTIONIST WHOSE TELEPHONE NUMBER IS (703) 308-0196.



DAVID ROMEO
PRIMARY EXAMINER
ART UNIT 1647

DSR
MARCH 20, 2005